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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,212	06/17/2005	Olga N. Kovbasnjuk	60384(71699)	2349

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EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
09/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,212	KOVBASNJUK ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-9,11,12 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-9,11,12 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/29/09 has been entered.

Claims 1-3, 6-9, 11-12 and 18 are pending.

The rejection under 35 U.S.C. 112, first paragraph, is withdrawn as stated in the advisory action.

The art rejection is withdrawn and re-written in favor of a new one.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-9, 11-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marcato et al Infection and Immunity vol. 70 p. 1279 (3/2002), in view of LaCasse et al Blood vol. 88 p. 1561 (1995) Strockbine et al J. Bacteriology vol. 170 p. 1116 (3/98), Accession Number 2002:397002 (3/2002), Green US 2002/0081307 and applicant's admission on page 6, lines 1-2 of the specification.

Marcato et al disclose shiga toxins 1 and its role in apoptosis. The A subunit inhibits protein synthesis thereby triggering apoptosis in lymphoma B cells in vitro. The B subunit alone also induces apoptosis but must be internalized to induce apoptosis in vitro. See abstract and entire reference.

This reference does not disclose the apoptosis in vivo and the limitations of claims 2, 6, 8-9, 11-12 and 18.

LaCasse et al disclose treatment of human B cell lymphoma from bone marrow in mice using Shiga-like toxin 1 (see entire reference). The reference also discloses that the toxin was administered after the cancer is present (see p. 1562, middle of first column). On page 6 of the specification, applicant admits the toxins are known to bind to Gb3 expressing cells, therefore it is expected that the cells of the reference are Gb3 expressing cells. The toxin is administered before the spread of the tumor and therefore prior to metastasis. The tumor killing occurs by inhibition of protein synthesis (page 1561-first column).

Strockbine et al discloses that Shiga-like toxin and Shiga Toxin are over 99% homologous and that the difference between the two resides in the A subunit (see abstract).

Green discloses that Shiga-like toxin (also called verotoxin) and Shiga toxin are commonly known and the selection of one or the other is within the purview of one skilled in the art and that either toxin can be used in mammals (this reads on humans). (see summary of invention).

Accession Number 2002:397002 discloses that Gb3 is a biomarker for colon tumor cells.

In view of the disclosure of Lacasse et al which shows in vivo use of shiga-like toxin to treat human B cell lymphomas and combined with the knowledge of Strockbine et al that shiga-like toxin and shiga toxin are over 99% homologous and the only difference resides in the A subunit (ie the B subunits are the same) and since both shiga-like toxin and shiga toxin both inhibit protein synthesis which results in cell death,

it would have been obvious to one of ordinary skill in the art at the time of applicant's invention that the A subunit is what causes inhibition of protein synthesis and that the B subunit (which can also induce apoptosis in vitro thru internalization) (Marcato et al) can also be used in vivo to inhibit apoptosis with the expected benefit of treating B cell lymphoma. This is obvious because (1) both shiga-like toxin and shiga toxin induce apoptosis, (2) the A subunit inhibits protein synthesis to induce apoptosis in vitro and therefore, in view of LaCasse et al which shows that shiga-like toxin inhibits protein synthesis in vivo to induce cell death it logically follows that it is the A subunit of shiga toxin that inhibits protein synthesis to induce apoptosis in vivo, and (3) therefore the B subunit which is identical in both the shiga-like toxin and the shiga toxin and which can induce apoptosis in vitro, that it can also induce apoptosis in vivo. Furthermore, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In view of this, it would have also been obvious to use other known cancer treatment, such as radiation or chemotherapeutic agents in combination with the B subunit to treat B cell lymphoma. Since Gb3 is a marker for colon caner and since the toxins bind Gb3, the B subunit can also be used to treat colon cancer.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Monday-Thursday 6am to 2pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sheela J Huff/
Primary Examiner
Art Unit 1643

sjh